

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
29 September 2005 (29.09.2005)

PCT

(10) International Publication Number
WO 2005/089753 A2

(51) International Patent Classification⁷: **A61K 31/423**,
C07D 413/12, 261/20, A61P 25/18

(74) Common Representative: **JANSSEN PHARMACEU-
TICA N.V.**; Turnhoutseweg 30, B-2340 Beerse (BE).

(21) International Application Number:
PCT/EP2005/051105

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(22) International Filing Date: 11 March 2005 (11.03.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
04101068.7 16 March 2004 (16.03.2004) EP
60/554,231 18 March 2004 (18.03.2004) US

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*):
JANSSEN PHARMACEUTICA N.V. [BE/BE]; Turn-
houtseweg 30, B-2340 Beerse (BE).

(72) Inventors; and

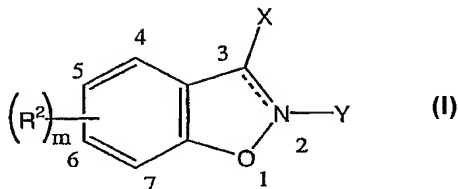
(75) Inventors/Applicants (*for US only*): **KENNIS, Ludo**,
Edmond, Josephine [BE/BE]; Janssen Pharmaceutica
N.V., Turnhoutseweg 30, B-2340 Beerse (BE). **VAN-
HOOF, Greta, Constantia, Peter** [BE/BE]; Janssen
Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse
(BE). **BONGARTZ, Jean-Pierre, André, Marc** [BE/BE];
Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340
Beerse (BE). **LUYCKX, Marcel, Gerebernus, Maria**
[BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg
30, B-BEERSE 2340 (BE). **MINKE, Wenda, Eveline**
[NL/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30,
B-2340 Beerse (BE).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ,*

[Continued on next page]

(54) Title: BENZISOXAZOLES



(57) Abstract: The present invention concerns the compounds of formula (I), the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein *m* represents an integer from 1 to 3; X represents amino, hydroxy, -oxo or -Z-R¹; Y is absent when X represents -Z-R¹ and -(C=O)-R⁶ when X represents oxo; Z represents carbonyl, -oxy-carbonyl- or -NR⁵-carbonyl-; R¹ represents C₁₋₄alkyl, Ar¹, Ar¹-C₁₋₄alkyl-, -NR³R⁴ or -Het¹; R² represents hydrogen, halo, nitro, hydroxycarbonyl-, C₁₋₄alkyloxy or C₁₋₄alkyl; R³ and R⁴ are each independently selected from hydrogen, Ar³ or C₁₋₄alkyl; R⁵ represents hydrogen,

C₁₋₄alkylcarbonyl- or Ar⁴-carbonyl-; R⁶ represents a substituent selected from the group consisting of C₁₋₄alkyl, Ar⁵, Ar⁶-C₁₋₄alkyl- or NR⁷R⁸; R⁷ and R⁸ are each independently selected from hydrogen, Het⁴ or C₁₋₄alkyl; Het¹ represents a heterocycle selected from oxazolyl, isoxazolyl, imidazolyl or pyrazolyl wherein said heterocycle is optionally substituted with one, two or three substituents selected from the group consisting of amino, C₁₋₄alkyl, hydroxy-C₁₋₄alkyl, phenyl, phenyl-C₁₋₄alkyl- and phenyl substituted with one or more halo substituents; Het⁴ represents a heterocycle selected from oxazolyl or isoxazolyl, wherein said heterocycle is optionally substituted with one or more substituents selected from the group consisting of amino, C₁₋₄alkyl, hydroxy-C₁₋₄alkyl-, phenyl, phenyl-C₁₋₄alkyl and phenyl substituted with one or more halo substituents; and Ar¹, Ar², Ar³, Ar⁴, Ar⁵ or Ar⁶ each independently represents phenyl optionally substituted one or where possible two or more substituents selected from halo, nitro, C₁₋₄alkyl, hydroxy or C₁₋₄alkyloxy-.



NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

- of inventorship (Rule 4.17(iv)) for US only

Published:

- without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.